Radiation stability of biocompatibile magnetic fluid

Natália Tomašovičová[1], Ivan Haysak[2], Martina Koneracká[1], Jozef Kováč[1], Milan Timko[1], Vlasta Závišová[1], Alexander Okunev[2], Alexander Parlag[2], Alexey Fradkin[2], Peter Kopčanský[1]
[1]Institute of Experimental Physics, Slovak Academy of Sciences, Watsonová 47, 04001 Košice, Slovakia
[2]Uzhgorod National University, Kapitulna 9A, 880 00 Uzhgorod, Ukraine

Abstract

The radiation stability of biocompatibile magnetic fluid used in nanomedicine after electron irradiation was studied. Two types of the water-based magnetic fluids were prepared. The first one was based on the magnetite nanoparticles stabilized by one surfactant natrium oleate. The second one was biocompatibile magnetic fluid stabilized with two surfactants, natrium oleate as a first surfactant and Poly(ethylene glycol) (PEG) as a second surfactant. The magnetization measurements showed that electron irradiation up to 1000Gy caused 50% reduction of saturation magnetization in the case of the first sample with only one surfactant while in the case of the second biocompatibile magnetic fluid, only 25% reduction of saturation magnetization was observed. In the first magnetic fluid the radiation caused the higher sedimentation of the magnetic particles than in the second case, when magnetic particles are covered also with PEG. The obtained results show that PEG behave as a protective element.

PACS nrs.:75.50.Mm; 61.80.Fe; 61.82.Rx

1 Introduction

Nanotechnology is beginning to allow scientist, engineers and physicians to work at the cellular and molecular levels to produce major advances in the life sciences and healthcare. Ferrofluids or magnetic fluids (dispersions of magnetic nanoparticles in liquids) belong to complex systems widely studied in modern nanoscience. Magnetic nanoparticles show remarkable phenomena such as superparamagnetism, high field irreversibility, high saturation field that make them very attractive for applications in biomedicine for example in drug targeting delivery, magnetic hyperthermia, arrangement of biological assemblies, contrast agents in Magnetic Resonance Imaging, biomagnetic separation [1]. Biomedical applications require the magnetic particles to be stable in water at neutral pH and physiological salinity. The colloidal stability of magnetic fluids [2, 3] will depend on the dimensions of particles, which should be sufficiently small to avoid of aggregation and on the surfactant commonly a monolayer of oleic acid (steric repulsion), or the particles are prevented from sticking to each other by electrostatic bilayer (electrostatic repulsion) [4, 5, 6, 7]. Moreover, for *in vivo* applications the magnetic particles must be coated with biocompatibile polymer [8, 9]. Magnetic hyperthermia is one of the widely studied application of magnetic fluids in medicine [10, 11, 12, 13]. In work [13], the combined thermotherapy and radiation with 20 Gy was shown to be significantly more effective than radiation with 20 Gy alone. Up to now there is very poor information about influence of radiation on the physical properties of the magnetic fluids. To our knowledge there is one publication [14] where influence of gamma radiation on magnetic properties of magnetic particles in the kerosene-based magnetic fluids. From the point of basic and applied research it is very important to study the physical properties and colloidal stability of magnetic fluids after radiation that are used for bioaplications. The aim of this paper was to study the stability of the magnetic properties of two types of water-based magnetic fluids suitable for bioaplications.

2 Experiment

The magnetic Fe_3O_4 particles were synthesized by a chemical co-precipitation procedure. Ferrous chloride heptahydrate ($FeSO_47H_2O$) and ferric chloride hexahydrate

($FeCl_36H_2O$) with molar ratio of 1:2 were dissolved in deionized water under vigorous stirring. Then 25 % w/v ammonium hydroxide (NH_4OH) was added as a base source at room temperature until pH value of 11 was reached. The sediment obtained was washed for five times with deionized water to remove impurities. The stabilization of the magnetite precipitate was achieved by adding natrium oleate ($C_{17}H_{33}COONa$), ratio 1.1 g to 1.5 g of Fe_3O_4 during stirring and heating until the boiling point was reached. Then centrifugation at 9000 rpm during 30 min followed. The system at this stage is investigated below as initial magnetic fluid. In a second magnetic fluid the poly(ethylene glycol) (PEG purchased from Sigma company) with chemical formula $C_{18}H_{33}NaO_2$ was used as a second surfactant with aim to increase the stability and improve the biocompatibility of the magnetic particles. Adsorption of PEG was carried out by adding PEG (Mw = 1000) to the magnetic fluid in the form of 10 % w/v water solution, while it was stirred and heated up to 50 °C. The mixture was stirred for one hour and then left to cool down to a room temperature. The added amount was 0.25 g of PEG per 1 g of Fe_3O_4. The prepared magnetic fluid contain 105 mg Fe_3O_4 /ml and the pH was 10.24.

With the aim to confirm the immobilization of natrium oleate and PEG to the magnetic particles, Fourier transform infrared (FTIR) spectra of the pure natrium oleate and PEG and after adsorption on the magnetite were measured by FTIR spectrometer FTLA2000 instrument (ABB, resolution 4 cm^{-1}) by the KBr pellet method. In this method, the solid sample is finely pulverized with pure and dry KBr, the mixture is pressed in a hydraulic press to form a transparent pellet, and the spectrum of the pellet is measured. Morphology and size distribution of prepared samples were obtained from transmission electron microscopy and Scanning electron microscopy (SEM). TEM showed nearly spherical shape of the magnetite core of the prepared magnetic fluids with average diameter 5 nm (Fig. 1). Fig. 2 shows the SEM image of the magnetic particles coated with natrium oleate and PEG.

The irradiation of samples was conducted by electrons on an accelerator "Microtron M-10" of Uzhgorod National University. The beam of electrons with energy 8.6 MeV was deflected in atmosphere through a thin titanic window. The samples in a glass container were exposed in the distance of 40 cm from the output window of the microtron. An intensity of the beam on this distance was set within the limits of

Φ=(1-8) $\times$ 10^9 electrons/cm^2 and was controlled by a thin-walled ionization chamber. The ionization chamber was calibrated by a Faraday cup the entrance window of which was disposed in the place of exposed patterns. This ionization chamber was used for measuring of dose in the process of irradiation too. For this purpose the output of the chamber was connected to an integrator of current. The value of absorbed dose was estimated by multiplying of electron fluence to a factor 3.3 $\times$ 10^{-9} Gy cm^2. The intensity of the electron beam during the process of irradiation remained stable within the limits of $\pm$ 5%.

The magnetization curves of the samples before irradiation and after irradiation with different doses were measured by SQUID magnetometer (Quantum Design MPMS 5XL) twice. The second measurement was done one month after first measurement. The upper part of the samples, kept in screw capped vials, was withdrawn for measurements. The weight of measured samples varied from the interval 20mg - 30mg. The error of weight was 4% that influence values of magnetization measurements.

The FTIR spectra of the samples before and after irradiation were measured by FTIR spectrometer FTLA2000 instrument (ABB, resolution 4 cm^{-1}) by Attenuated Total Reflectance measurements with diamond window. For infrared measurements the samples were first mixed and than dried.

3 Results and discussion

The prepared samples, water-based magnetic fluid containing magnetic particles coated with natrium oleate and water-based magnetic fluid containing magnetic particles coated with natrium oleate as a first surfactant and PEG as a second surfactant were irradiated with different fluences 1.65×10^{10}, 6.6×10^{10}, 3.3×10^{11}, 1.65×10^{12}, 3.3×10^{12} electrons/cm^2 that corresponds doses 5Gy, 20Gy, 100Gy, 500Gy and 1000Gy, respectively.

All studied samples were placed in the screw capped vials. One week after irradiation the upper parts of magnetic fluids were withdrawn for magnetisation measurements. The magnetization curves of the samples before irradiation and after irradiation with different doses of the magnetic fluid containing magnetic nanopar-

Table 1: The saturated magnetization (in mT) of the sample with one surfactant before and after irradiation obtained from the first measurements and from the measurements after one month.

dose	0Gy	5Gy	20Gy	100Gy	500Gy	1000Gy
1^{st}	4.02	2.54	2.16	2.14	2.08	2.22
2^{nd}	4.01	2.55	2.18	2.12	2.10	2.10

ticles coated with one surfactant (natrium oleate) and magnetic fluid containing magnetic particles coated with two surfactants (natrium oleate and PEG)are shown in Fig. 3 and Fig. 4, respectively. The obtained results shoved significant reduction of magnetization after irradiation of 5Gy. The next increase of the dose influence the magnetization only slightly. The similar behaviour was observed for both magnetic fluids.

Fig. 5 and Fig. 6 show the reduction of the saturated magnetization for the irradiated samples. From this figures is clearly seen that the electron irradiation up to 20 Gy caused 50% reduction of the saturation magnetization in the case of the sample with only one surfactant while in the case of the second biocompatibile magnetic fluid coated also with PEG, only 25% reduction of the saturation magnetization was observed. The obtained results show that in the first magnetic fluid the irradiation caused the higher sedimentation of the magnetic particles than in the second one, when magnetic particles are covered also with PEG. From these figures is also seen that there is no additional reduction in the saturated magnetization after irradiation with higher doses up to 1000Gy.

The second measurement of the magnetisation was done one month after the first measurement. The samples for the measurement were prepared the same way as for the first measurement. In Tab. 1 and Tab. 2 are summarized the saturated magnetizations obtained from the first and from the second magnetisation measurements of the sample with one surfactant and the sample with two surfactants, respectively. The obtained results show no change in the saturation magnetization after one month. These results show that after sedimentation process that occur after irradiation, there is no additional sedimentation and all samples are time stable.

As possible mechanisms of magnetism degradation after irradiation can be considered nuclear reactions, ionization processes and degradation of surfactant molecules.

Table 2: The saturated magnetization (in mT) of the sample with two surfactants before and after irradiation from the first measurements and form the measurements after one month.

dose	0Gy	5Gy	20Gy	100Gy	500Gy	1000Gy
1^{st}	2.65	2.07	1.78	1.77	1.88	1.88
2^{nd}	2.65	2.10	1.85	1.75	1.74	1.82

However, there are no nuclear reaction at the used electron energy 8MeV. So the only possible processes at the used electron energy are ionization and molecules destroying that could lead to the aggregation of the particles. On the other hand, the decrease of magnetization has saturating behaviour and after sedimentation that occurs after irradiation there is no additional sedimentation and samples are time stable.

Fig. 7 and Fig. 8 show the infrared spectra of magnetic particles coated only with natrium oleate and magnetic particles coated with natrium oleate and PEG, respectively. The spectra are shifted vertically for clarity. The all absorption bands corresponding the natrium oleate or PEG as well as the band observed at 584 cm^{-1}, which corresponds to the magnetite, before irradiation and after irradiation are identical. These results clearly indicate that the molecules of the surfactants as well as the magnetite particles are stable under irradiation and no destroying processes occur due to the irradiation. It seems that ionization can be mainly responsible for aggregation of the particles.

4 Conclusion

In summary, the magnetization measurements showed that electron irradiation up to 1000Gy caused 50% reduction of saturation magnetization in the case of the sample with only one surfactant. In the case of the second biocompatibile magnetic fluid, only 25 % reduction of the saturation magnetization was observed. The obtained results showed that the radiation causes aggregation of the particles and consequently their sedimentation. The infrared spectra confirmed that the process that causes the sedimentation after irradiation is ionization. However, in the case when magnetic particles were covered also with PEG, the obtained results showed that PEG behave as a protective element. Moreover, after first sedimentation process that occurs after

irradiation, there is no further sedimentation and the sample with one surfactant as well as the sample with two surfactants are time stable.

Acknowledgments

This work was supported by the Ministry of Education and Science of Ukraine in the framework of project DB-715, by the Slovak Academy of Sciences, in the framework of CEX-NANOFLUID, projects VEGA 0077 and 0311, APVV 0509-07 and Ministry of Education Agency for Structural Fonds of EU in frame of project 6220120021 and 26220220005.

References

[1] A.Q. Pankhurst, N.K.T. Thanh, S.K. Jones, J. Dobson, J. Phys.D: Appl. Phys. 42 (2009) 224001

[2] A.P. Herrera, C. Barrera, Y. Zayas, C. Rinaldi, J. Colloid Interface Sci. 342 (2010) 540

[3] E.S. Kooij, A.C. Galca, B. Poelsema, J. Colloid Interface Sci. 327 (2008) 261

[4] M. Latorre-Esteves, A. Cortes, M. Torres-Lugo, C. Rinaldi, J. Magn. Magn. Mater.321 (2009) 3061

[5] M.V. Avdeev, D. Bica, L. Vekas, V.L. Aksenov, A.V. Feoktystov, O. Marinica, L. Rosta, V.M. Garamus, R. Willumeit, J. Colloid Interface Sci. 334 (2009) 37

[6] D. Bica, L. Vekas, M.V. Avdeev, O. Marinica, V.Socoliuc, M. Balasoiu, V.M. Garamus, J. Magn. Magn. Mater.311 (2007) 17

[7] M.V. Avdeev, V.L. Aksenov, M. Balasoiu, V.M. Garamus, A. Schreyer, G. Torok, L. Rosta, D. Bica, L. Vekas, J. Colloid Interface Sci. 295 (2006) 100

[8] S.I. Park, J.H. Lim, H.I. Yun, J.S. Roh, C.G. Kim, C.O. Kim, Phys. Status Solidi B 241 (2004) 1662

[9] M. Chanana, Z.W. Mao, D.Y. Wang, J. Biomedical Nanotechnology 5 (2009) 652

[10] I. Apostolova and J.M. Wesselinova, Phys. Status Solidi B **246**, 1925 (2009).

[11] A. Jordan, R. Scholz, K. Maier-Hauff, M. Johannsen, P. Wust, J. Nadobny, H. Schirra, H. Schmidt, S. Deger, S. Loening, W. Lanksch, R. Felix, J. Magn. Magn. Mater. 225 (2001) 118

[12] M. Johannsen, U. Gneveckow, L. Eckelt, A. Feussner, N. Waldofner, R. Scholz, S. Deger, P. Wust, S.A. Loening, A. Jordan, Int.J.Hyperthermia 21 (2005) 637

[13] M. Johannsen, B. Thiesen, U. Gneveckow, K. Taymoorian, N. Waldofner, R. Scholz, S. Deger, K. Jung, S.A. Loening, A. Jordan, Prostate 66 (2006) 97

[14] P. Kopcansky, J. Cernak, T. Tima, A. Zentko, M. Timko, P. Slanco, J. Magn. Magn. Mater. 85 (1990) 103

[15] M. Koneracka, P. Kopcansky, P. Sosa, J. Bagelova, M. Timko, J. Magn. Magn. Mater. 293 (2005) 271

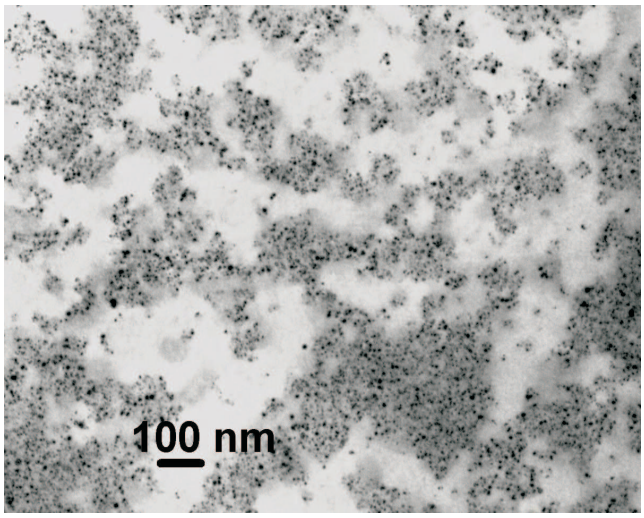

Figure 1: TEM image of magnetite nanoparticles.

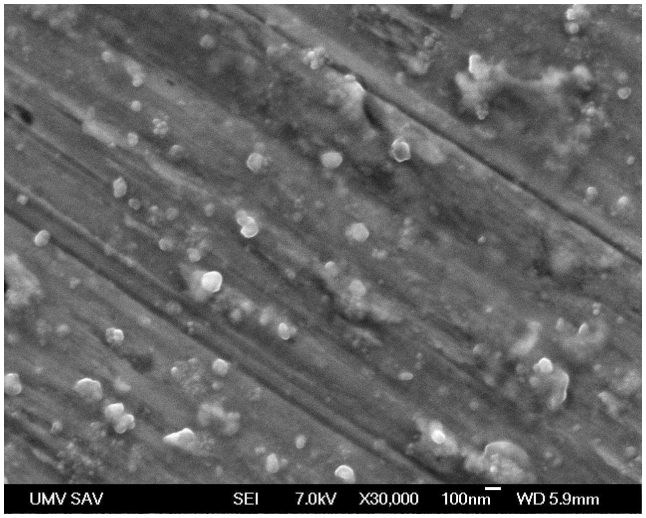

Figure 2: SEM image of magnetic nanoparticles coated with natrium oleate and PEG.

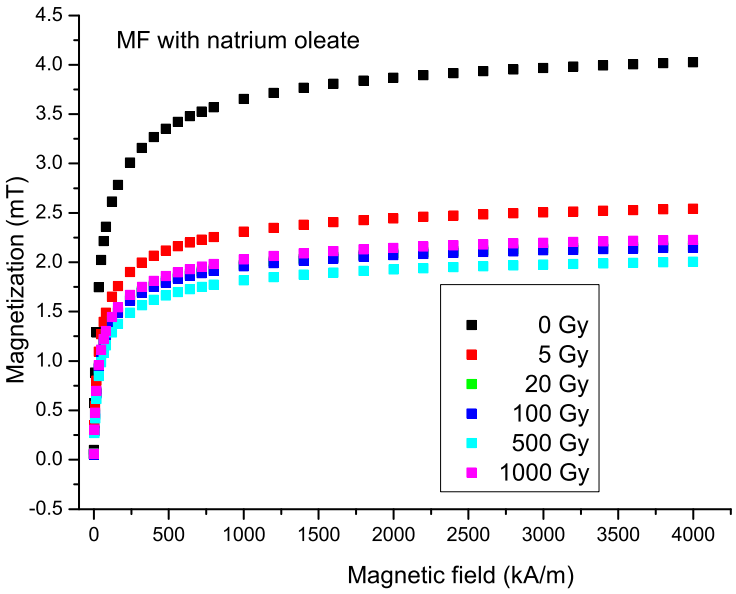

Figure 3: Magnetization curves of the water-based magnetic fluid containing the magnetic particles coated with natrium oleate before and after irradiation with different doses.

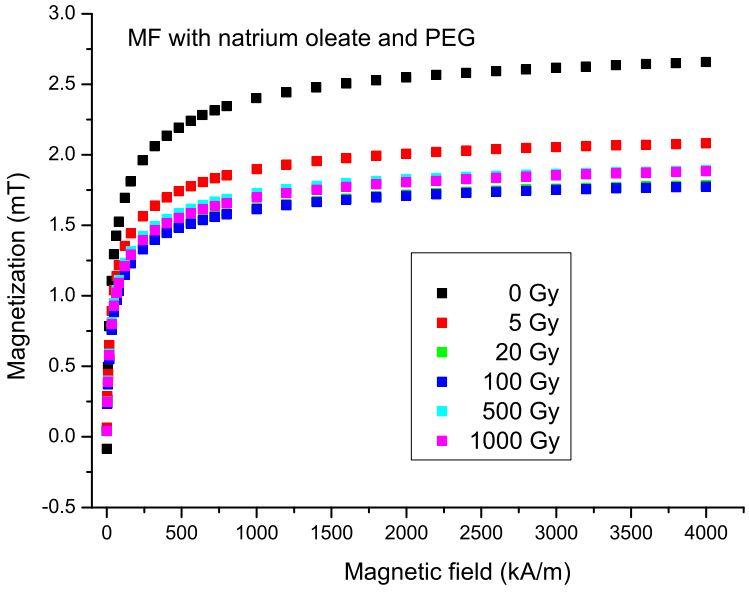

Figure 4: Magnetization curves of the water-based magnetic fluid containing the magnetic particles coated with natrium oleate and PEG before and after irradiation with different doses.

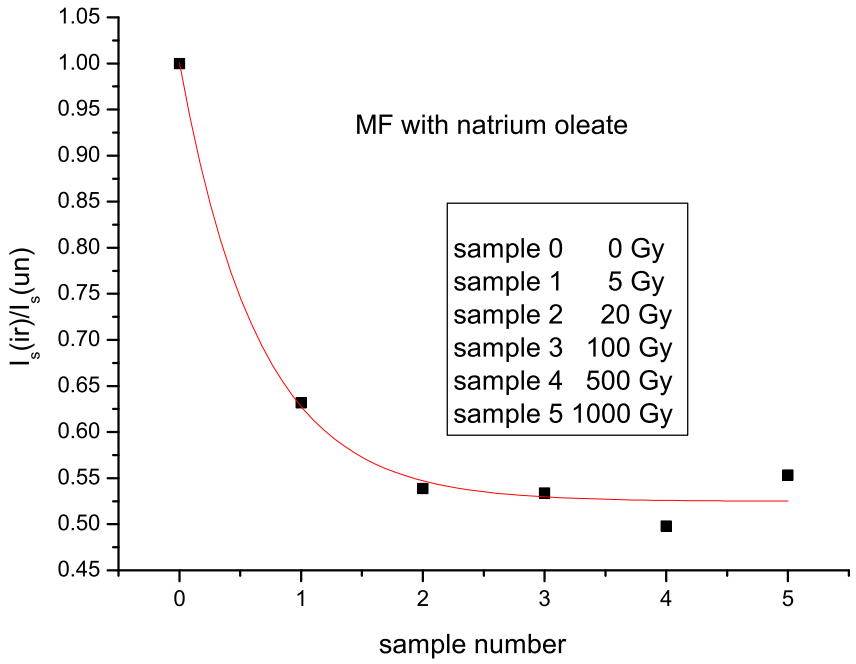

Figure 5: Dependence of reduced saturation magnetization on irradiation doses of water-based magnetic fluid containing magnetic particles coated with natrium oleate. The solid line is for eyes.

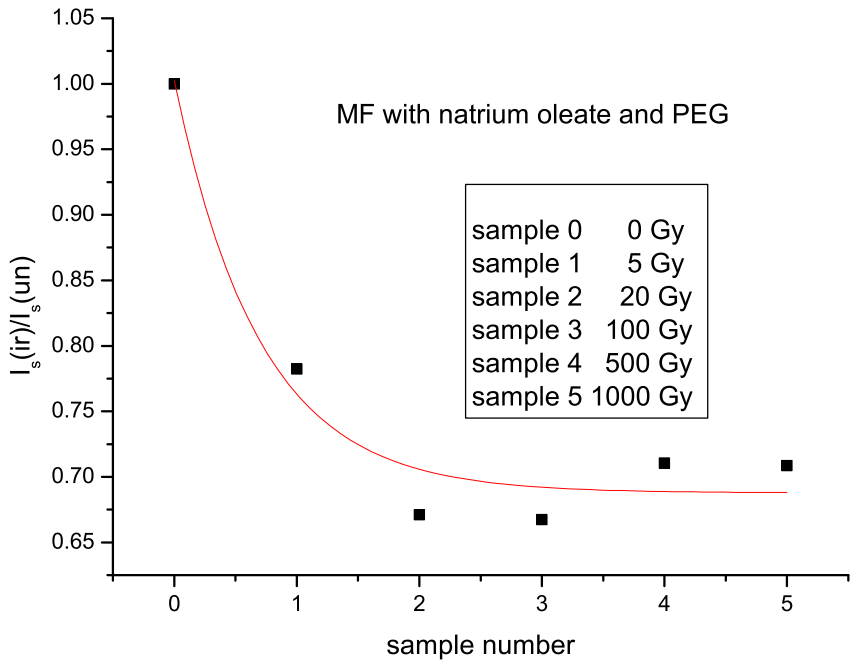

Figure 6: Dependence of reduced saturation magnetization on irradiation doses of water-based magnetic fluid containing magnetic particles coated with natrium oleate and PEG. The solid line is for eyes.

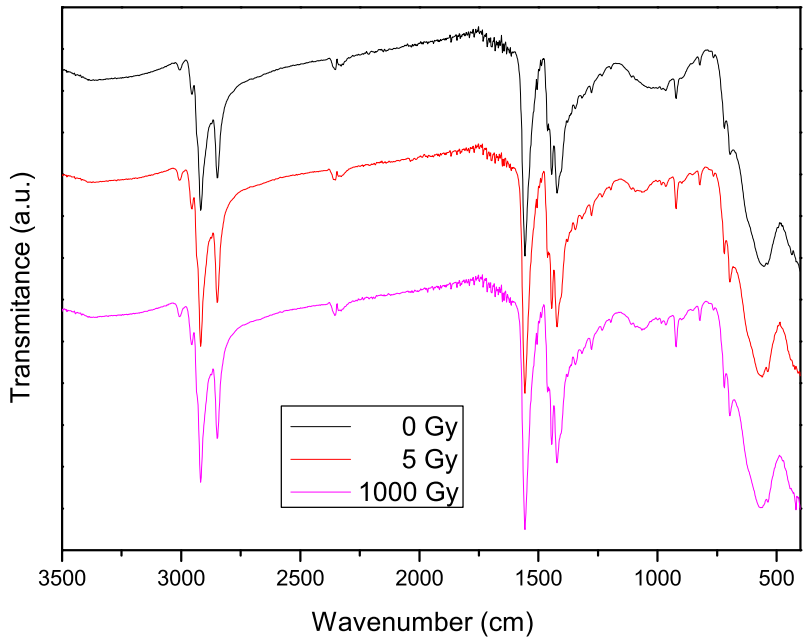

Figure 7: FTIR spectra of magnetite coated with natrium oleate before irradiation and after irradiation with 5Gy and 1000Gy. The spectra are shifted vertically for clarity.

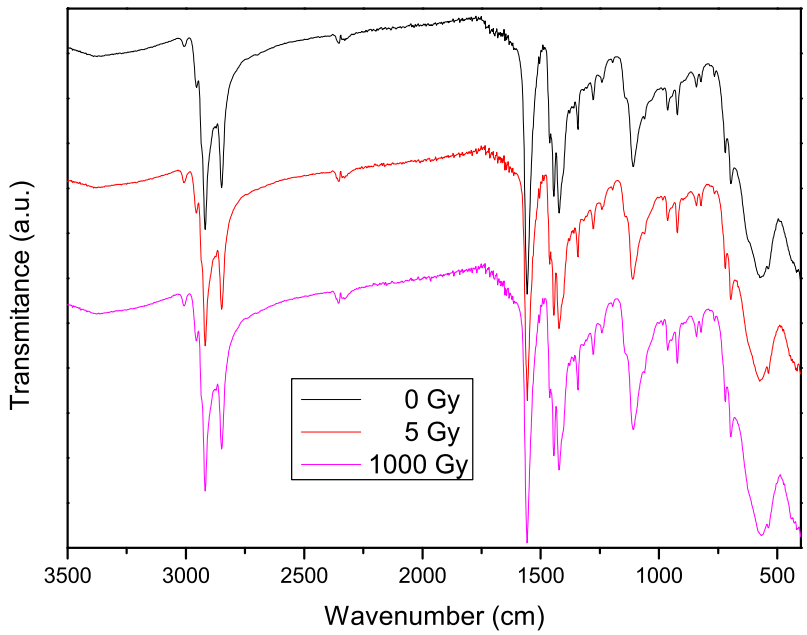

Figure 8: FTIR spectra of magnetite coated with natrium oleate and PEG before irradiation and after irradiation with 5Gy and 1000Gy. The spectra are shifted vertically for clarity.